

Favorable impact of allogeneic stem cell transplantation in patients with therapy-related myelodysplasia regardless of *TP53* mutational status

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Supplement Figure Legends:

Supplement Figure 1. TP53 mutations plot.

Supplement Figure 2. (a) OS, and (b) RFS for t-MDS patients with TP53-wild (solid line), one TP53 mutation (dashed line), and more than 1 TP53 mutation (dotted line).

Supplement Figure 3. The frequency of additional CNV abnormalities and LOH regions identified by microarray compared to conventional analysis.

Supplement table 1- List of sequenced genes

<i>ASXL1</i>	<i>CBLB</i>	<i>DNMT3A</i>	<i>IDH1</i>	<i>KMT2A</i>	<i>NOTCH1</i>	<i>PTPN11</i>	<i>TET2</i>
<i>ATM</i>	<i>CCND1</i>	<i>EP300</i>	<i>IDH2</i>	<i>KMT2C</i>	<i>NOTCH2</i>	<i>RUNX1</i>	<i>TNFAIP3</i>
<i>BCOR</i>	<i>CCND3</i>	<i>ETV6</i>	<i>IKZF1</i>	<i>KMT2D</i>	<i>NPM1</i>	<i>SETBP1</i>	<i>TP53</i>
<i>BIRC3</i>	<i>CD79A</i>	<i>EZH2</i>	<i>IL7R</i>	<i>KRAS</i>	<i>NRAS</i>	<i>SF3B1</i>	<i>U2AF1</i>
<i>BRAF</i>	<i>CD79B</i>	<i>FBXW7</i>	<i>JAK1</i>	<i>MEF2B</i>	<i>PAX5</i>	<i>SPI1</i>	<i>UBR5</i>
<i>BTK</i>	<i>CDKN2A</i>	<i>GATA1</i>	<i>JAK2</i>	<i>MIR142</i>	<i>PDGFRA</i>	<i>SRSF2</i>	<i>WHSC1</i>
<i>CALR</i>	<i>CEBPA</i>	<i>GATA2</i>	<i>JAK3</i>	<i>MPL</i>	<i>PHF6</i>	<i>STAG2</i>	<i>WHSC1L1</i>
<i>CARD11</i>	<i>CREBBP</i>	<i>HRAS</i>	<i>KDM6A</i>	<i>MYC</i>	<i>PIK3CA</i>	<i>SUZ12</i>	<i>WT1</i>
<i>CBL</i>	<i>CSF3R</i>	<i>ID3</i>	<i>KIT</i>	<i>MYD88</i>	<i>PTEN</i>	<i>TCF3</i>	<i>ZRSR2</i>

Supplement table 2- List of variants with VAF and coverage

SampleID	Chr	Gene	Coding change	Amino acid change	Coverage	Frequency
2101	17	TP53	c.818G>A	p.Arg273His	1727	38.6
2229	18	SETBP1	c.244G>T	p.Ala82Ser	872	45.6
2229	18	SETBP1	c.2608G>C	p.Gly870Arg	631	39.9
2229	4	TET2	c.1397delT	p.Leu467fs	1103	36.6
5038	4	TET2	c.4609C>T	p.Arg1537*	1677	8.4
5132	18	SETBP1	c.244G>T	p.Ala82Ser	2192	46.2
5132	18	SETBP1	c.2608G>C	p.Gly870Arg	1780	38.4
5132	4	TET2	c.1397delT	p.Leu467fs	1555	37.2
5804	17	TP53	c.817C>A	p.Arg273Ser	1291	10.8
7395	2	DNMT3A	c.2077C>T	p.R693C	1527	22.5
7395	12	PTPN11	c.925A>G	p.Ile309Val	1393	46.4
7395	21	RUNX1	c.552_553insT	p.Asp185fs	1388	12.1
7395	21	U2AF1	c.470A>G	p.Gln157Arg	1695	11.4
3766	12	PTPN11	c.215C>T	p.Ala72Val	1545	11.7
3766	21	RUNX1	c.521G>A	p.Arg174Gln	2244	41.7
4477	20	ASXL1	c.1928_1929insC	p.Gly646fs	1657	39.7
5971	17	TP53	c.796G>C	p.Gly266Arg	383	15.9
5971	17	TP53	c.994-1G>GA	Splice	2220	16.1
5971	21	U2AF1	c.101C>T	p.Ser34Phe	844	5.9
6027	20	ASXL1	c.1762C>T	p.Gln588*	938	9.7
6027	7	EZH2	c.2084C>T	p.S695L	821	10.5
7205	21	RUNX1	c.351+1G>GA	Splice	2042	14.3
0303	11	ATM	c.5821G>C	p.Val1941Leu	965	44.6
6391	X	STAG2	c.1535-2_1535-1insA	Splice	1093	18.6
6678	21	RUNX1	c.254T>C	p.Leu85Pro	1431	18.6
7837	21	RUNX1	c.520C>T	p.Arg174*	1631	30.9
7837	17	TP53	c.743G>A	p.Arg248Gln	1081	47.5
0389	7	EZH2	c.475G>A	p.Gly159Arg	475	48.4
4035	12	KMT2D	c.15621delC	p.Val5208fs	1688	5.6
6622	17	TP53	c.517G>A	p.Val173Met	1963	32.5
8256	4	TET2	c.1124C>G	p.Ser375*	2945	5.9
8256	17	TP53	c.920-2A>GA	Splice	4037	10.0
			c.1968_1998delCCAG CATTTTCCTGTCTTCAT			
1482	2	DNMT3A	GAATGAGAAA	p.D656fs*26	1656	8.2
			c.965_1009+15delTCT CCCCGCCTGAAGAGCA CGCCATGCCATTGGG AGAATAGCAGGTGAG			
1482	12	ETV6	TGAGTTCCCC	p.Val322_Ala336del	1375	7.1
6160	17	TP53	c.713G>A	p.Cys238Tyr	2320	16.7

SampleID	Chr	Gene	Coding change	Amino acid change	Coverage	Frequency
6160	17	TP53	c.673- 7_674delCTCCTAGGT	p.Val225fs	1856	15.5
6160	17	TP53	c.673-2_674delAGGT	Splice	2369	15.2
7212	17	TP53	c.80delC	p.Pro27fs	1090	16.5
7212	17	TP53	c.614A>C	p.Tyr205Ser	2388	19.5
7551	11	CBL	c.1027C>T	p.Arg343*	1698	12.0
7551	2	SF3B1	c.1997A>C	p.Lys666Thr	2055	29.9
7551	17	SRSF2, MF5	c.284C>A	p.P95H	1645	19.5
7677	21	RUNX1	c.413G>T	p.Gly138Val	1628	7.3
			c.9_32dupGGCGGCGG GGAGCAGCATGGAGC			
7763	9	CDKN2A	C	p.A4_P11dup	786	6.2
7763	12	PTPN11	c.1658C>T	p.Thr553Met	1027	44.9
0140	17	TP53	c.524G>A	p.Arg175His	1985	12.9
0140	17	TP53	c.856G>A	p.Glu286Lys	1636	12.8
1077	2	DNMT3A	c.2077C>T	p.R693C	1818	46.7
1077	17	SRSF2, MF5	c.284C>A	p.P95H	1139	27.2
1372	17	TP53	c.747G>C	p.Arg249Ser	2635	35.6
1372	17	TP53	c.394A>G	p.Lys132Glu	1989	37.4
4772	17	TP53	c.818G>A	p.Arg273His	733	67.8
6645	17	TP53	c.711G>A	p.Met237Ile	1388	51.2
			c.329_338delGTCTGG	p.Arg110_Phe113deli		
6798	17	TP53	GCTTinsA	nsHis	360	61.4
1231	X	PHF6	c.287delT	p.Val96fs	904	41.8
1757	21	RUNX1	c.211delC	p.Leu71fs	1597	8.5
1757	17	TP53	c.733G>A	p.Gly245Ser	2420	54.3
			c.1951_1958delGGCG			
5226	20	ASXL1	GCGG	p.Gly652fs	1384	48.0
5226	21	U2AF1	c.470A>C	p.Gln157Pro	1925	39.6
			c.1122_1131delCAGC			
5226	X	ZRSR2	AGGCTG	p.Ser375fs	949	70.7
5226	X	ZRSR2	c.558-1G>CG	Splice	886	9.8
2239	4	TET2	c.3979delC	p.Gln1327fs	700	7.0
2239	21	U2AF1	c.101C>T	p.Ser34Phe	829	8.3
			c.2455_2456insGAGA			
4802	20	ASXL1	T	p.Asp821fs	2366	28.1
4802	9	JAK2	c.1849G>T	p.Val617Phe	1252	58.3
4802	17	TP53	c.714_715insGT	p.Asn239fs	2066	27.9
406	17	TP53	c.824G>A	p.Cys275Tyr	1004	6.2
0844	11	CBL	c.1250C>G	p.Pro417Arg	2644	29.7
0844	18	SETBP1	c.2607C>A	p.Ser869Arg	3011	15.3
3167	X	STAG2	c.3092_3093insA	p.Leu1032fs	873	5.7

SampleID	Chr	Gene	Coding change	Amino acid change	Coverage	Frequency
3167	17	TP53	c.551_554delATAG	p.Asp184fs	5596	25.2
5527	20	ASXL1	c.1926_1927insG	p.Gly646fs	1483	34.2
5527	12	ETV6	c.313C>G	p.Arg105Gly	1450	37.8
5527	3	GATA2	c.1187G>A	p.Arg396Gln	2136	42.1
5527	1	NRAS	c.34G>A	p.Gly12Ser	1604	44.1
5527	18	SETBP1	c.2608G>A	p.Gly870Ser	1517	42.4
5527	21	U2AF1	c.470A>C	p.Gln157Pro	2438	42.4
1607	11	KMT2A	c.82delG	p.Gly29fs	24	8.3
T513	17	TP53	c.817C>T	p.Arg273Cys	1406	53.2
9107	2	DNMT3A	c.1815C>A	p.F605L	1370	12.8
9765	17	TP53	c.747G>C	p.Arg249Ser	3313	27.9
9765	17	TP53	c.782+1G>GA	Splice	5764	32.0

Supplement table 3- Microarray results

	Cytogenetics/FISH	Cytogenomic Microarray (CMA)^{1&2}	Description of CMA added value
1	Stemline: 43,X,-Y,-5,-7,dic(12;18)(p12.2;p11.2),+r1 [15 /20]Sideline: 44,idem,+r2 [5 /20]	- 5p15.33p13.3(113,576-31,155,754)x1-2 - 5q23.1q35.3(118,618,699-180,719,789)x1-2 - 7p22.3q36.3(43,360-159,119,707)x1 - 12p13.33(173,786-2,612,192)x1-2 - 12p13.32(3,436,758-4,990,196)x3 - 12p13.32p13.31(4,990,825-5,925,341)x2-3 - 12p13.31p12.1(5,936,101-23,910,093)x1-2 - 17p13.3p11.1(18,900-22,217,883) hmz ³ - 18p11.32(136,226-1,374,335)x1-2 - 18p11.32p11.21(1,373,923-14,734,334)x1-2 - Yp11.31q11.23(2,650,140-28,799,937)x0-1	5p and 5q loss rather than -5. 12p and 18p have complex losses/gains. 17p LOH involving <i>TP53</i> .
2	Stemline: 47,XX,del(1)(p34.3p36.1),del(5)(q13q35),+8,t(15;21)(q15;q22.3) [20 /20]	- 1p36.32p35.2(2,458,619-30,351,602)x1-2 - 5q14.2q34(82,375,769-165,838,507)x1-2 - 8p23.3q24.3(158,048-146,295,771)x2-3	None
3	Stemline: 46,XY,t(3;12)(p25;q13) [16/20]	Normal study	None
4	Stemline: 45,XY,t(2;19)(p13;q13.1),t(3;8)(p25;q13),-7,?del(17)(q21q22),add(20)(p13) [24/27]	- 2p16.1p14(55,640,032-65,276,312) hmz - 7p22.1p11.2(7,198,130-56,223,838)x1-2 - 7q22.1q36.3(99,171,842-159,119,707)x1-2 - 8p22p21.2(13,707,775-23,551,121) hmz - 11q25(134,355,932-134,764,922)x3-4 - 12q21.31q21.32(85,924,926-87,979,453)x1-2	LOH on 2p and 8p, small gain on 11q and loss on 12q. Large 7p and 7q losses rather than -7.
5	Stemline: 47,XX,+21[15/20]. 8.3% trisomy 21 by FISH.	Trisomy 21	None
6	Previous Stemline: 45,XX,del(5)(q15),-6,der(7)t(?2;7)(q21;p15),-18,+mar[1/20]	- 2q21.2(132,721,612-133,358,558)x3 - 4q13.2q13.3(68,739,143-72,269,733) hmz	3.5 Mb LOH on 4q involving 49 genes, small gain on 2q.
7	Stemline: 45,XY,-7,del(12)(p11.2p13)[2] Constitutional Cell Line: 46,XY[2/20]	- 6p11.2(57,215,493-57,641,858)x3 - 7p22.3q36.1(2,761,829-152,239,258)x1-2 - 12p13.31p11.21(9,293,420-31,869,307)x1-2	Small 6p gain involving only 1 gene (<i>PRIM2</i>).
8	Stemline: 45,XY,-5,add(17)(p11.2),-18,+mar[6/20]	- 5p12q12.3(43,301,512-65,550,256)x1-2 - 5q14.1q35.3(79,393,143-180,719,789)x1-2 - 6q14.1(78,336,648-78,749,628)x3 - 10q11.21q11.22(44,815,708-48,364,115) hmz - 17p11.2(17,352,340-20,640,934) hmz - 17p13.3p12(525-14,003,182)x1-2 - 18p11.32p11.31(136,226-7,089,771)x1-2 - 18q11.2q23(23,627,402-78,014,123)x1-2	Confirmed <i>TP53</i> deletion. Array data indicates marker is likely der(18). 5p and 5q have large losses rather than monosomy 5. 10q LOH containing 75 genes and 17p LOH containing 117 genes.
9	46,XX	- 5q35.2q35.3(173,749,574-177,902,889) hmz	4 Mb LOH on 5q containing 61 genes including <i>NSD1</i> (mutated in Sotos and Weaver syndrome), <i>DDX41</i> and <i>NHP1</i> .
10	Stemline: 46,XX,t(1;17)(p36.3;q23)[2/20]	Normal study	None
11	Stemline: 45,XY,-7[13/20] FISH positive for monosomy 7 at 34%	- 7p22.3q36.3(43,360-159,119,707)x1-2	None
12	46,XX,inv(11)(p15q22)[21]	Normal study	None

13	Stemline: 45,XX,-7,i(22)(q10)[14/20] Sideline: 45,X,del(X)(q24q28),-7[8/20]	- 7p22.3q36.3(43,360-159,119,707)x1-2 - 17q11.2(26,254,603-31,087,928)x1-2 - 19p13.3p13.11(260,911-17,387,176) h mz - 22q11.1q13.33(16,888,899-51,197,838)x2-3 - Xp22.33p11.1(168,546-58,368,204)x3	17q loss involving 102 genes namely <i>NF1</i> . Large LOH on 19p involving 529 genes.
14	46,XX [20]	- 9q34.11(132,449,936-132,795,093)x3 - 17q25.3(78,366,131-78,398,120)x1	Small gains on 9p and 17q with unknown significance.
15	Stemline: 46,XX,del(7)(q22),add(18)(p11.2),inv(18)(q21.1q23)[20]	- 1p12p11.2(120,549,228-120,606,931)x1-2 - 3q26.2q29(170,650,651-197,851,986)x2-3 - 7q21.12q36.3(88,109,148-159,119,707)x1-2 - 15q11.2(22,770,421-23,291,159)x2-3 - 18p11.32p11.21(136,226-12,039,463)x1-2 - 18q12.1(28,769,131-31,940,611) h mz - 18q21.2q23(49,708,959-78,014,123)x1-2 - 21q22.13q22.3(38,189,113-48,097,372)x3-4	Several large gains and losses on 3q, 18q and 21q as well as an LOH on 18q. Loss of exon 2 of <i>NOTCH2</i> on 1p.
16	46,XX	- 1p12p11.2(120,549,754-120,611,245)x1-2	Loss of exon 2 of <i>NOTCH2</i> on 1p.
17	46,XX,?Add(15)(q24)[2/20]	- 3p22.2p21.31(36,597,900-46,366,324) h mz	9.7 Mb LOH on 3p involving 169 genes such as <i>MLH1</i> .
18	FISH positive for del(5) (9.5%) and trisomy 8 (16%)	Normal study	None
19	Stemline: 46,XY,t(1;16)(q21;p13.3),der(2)?T(2;11)(p23;q23)del(2)(q33q37),add(4)(p14),add(5)(q11.2),add(6)(p23),del(10)(q22q24),der(11)t(2;11),?Del(13)(q12q22)[2/30]	- 13q12.12q12.2(24,721,630-28,881,335) h mz - 13q12.3q13.2(30,750,386-35,155,254) h mz	Two adjacent LOH regions involving several genes such as <i>PAN3</i> , <i>FLT3</i> , <i>CDX2</i> , <i>BRCA2</i> , <i>HSPH1</i> , <i>PDS5B</i> , and <i>STARD13</i> .
20	46,XX [19/20]	- 7p22.3q36.3(43,360-159,119,707)x1-2 - Xq26.2q26.3(130,793,578-133,944,050) h mz	Monosomy 7. LOH on Xq involving <i>GPC3</i> and <i>PHF6</i> .
21	Stemline: 46,XX,del(2)(q3?2q35),del(7)(q21.2q22.3),r(11)(p13q23)[2/20] Sideline: 46,sl,t(X;16)(p11.2;q22),del(13)(q12q22)[11/20]	- 2q32.1q37.3(188,400,999-242,783,384)x1-2 - 7q22.1q22.3(98,648,364-106,197,812)x1-2 - 11p15.1p12(19,640,816-39,620,383)x1-2 - 11p12q14.1(39,795,927-82,850,496)x2-3 - 11q14.1q25(83,231,956-134,938,470)x1-2 - 13q13.1q21.33(32,627,618-69,403,994)x1-2	Large losses on 11p and 11q as well as trisomy of the resultant der(11).
22	46,XY	Normal study	None
23	46,XY,r(7)(p15q22)[20]. FISH positive for del(7) (67.5%)	- 4q32.1(156,453,560-161,751,904) h mz - 7p22.3p11.2(43,360-56,679,833)x1-2 - 7q21.13q36.3(90,333,513-159,119,707)x1-2 - 20q11.21q11.22(29,448,795-32,629,322) h mz	LOH on 4q and 20q including <i>ASXL1</i> .
24	Stemline: 47,XX,+15[12/20]	- 2q22.1q22.3(139,802,110-148,374,082) h mz - 3q12.3q13.11(102,246,060-105,914,183) h mz - 4q32.1q32.2(157,612,290-162,375,382) h mz - 5q14.3(83,003,741-88,002,445) h mz - 17p11.2p11.1(18,860,660-22,217,883) h mz - 17q11.1q11.2(25,309,336-28,687,196) h mz	Several LOH blocks on chromosomes 2q, 3q, 4q, 5q, 17p and 17q.
25	del20q per outside report	- 7q34q36.3(142,918,614-159,119,707)x1-2 - 8p23.3p23.2(158,048-3,258,947)x2-3 - 10q26.2q26.3(128,877,541-135,427,143)x2-3 - 16q11.2q24.3(46,463,672-90,155,062)x1-2 - 17p13.3p11.1(1,397,388-22,261,792)x1-2 - 20q11.23q13.31(36,339,323-56,296,530)x1-2	Large gains 8p and 10q. Large losses on 7q, 16q and 17p. The latter loss involves <i>TP53</i> .

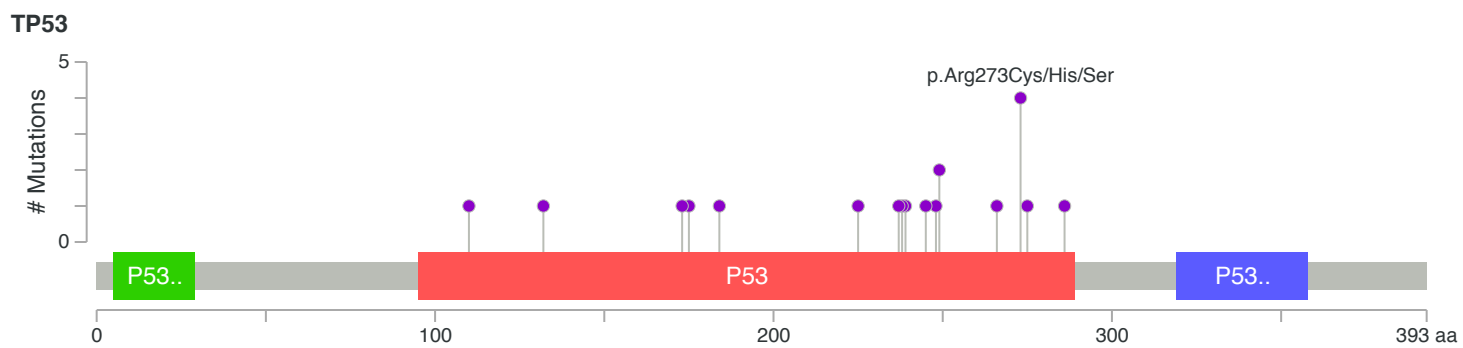
26	del5,mono12,add 12p per outside report	<ul style="list-style-type: none"> - 5q11.2q33.2(52,418,898-154,787,663)x1-2 - 12q14.3(65,178,751-66,533,363)x3 - 12q14.3q15(67,635,402-71,180,545)x2-3 - 12q21.1(72,203,588-72,915,302)x3 - 12q21.1(72,915,349-75,033,481)x2-3 - 12q21.1q21.2(75,051,120-76,379,095)x2-3 - 12q21.2q24.32(76,387,175-128,682,425)x1-2 - 12q24.32q24.33(128,685,658-132,696,025)x2-3 - 12q24.33(132,811,668-133,777,902)x1-2 - 17p13.3p13.1(272,528-7,512,922)x1-2 - 17p13.1q12(8,827,926-34,477,480)x1-2 	Very complex rearrangement of 12q containing several tandem gains flanking a large loss. Loss on 17p.
27	46,XY	<ul style="list-style-type: none"> - 1q21.3q23.2(154,945,046-159,833,733) hmz - 6p12.1p11.1(55,395,819-58,741,497) hmz - 6q11.1q12(61,968,745-67,820,187) hmz - 6q14.1q14.3(82,721,983-86,094,187) hmz - 8p12p11.23(31,123,340-37,085,115) hmz - 13q14.13(46,713,528-46,738,835)x1 	Several LOH regions on chromosomes 1q, 6p, 6q and 8p. A small loss on 13q involving <i>LCP1</i> .
28	46,XX	- 15q11.2(22,770,421-23,288,350)x3	Likely constitutional gain on 15q involving 16 genes.
29	47,XY,+8[20]	- 8p23.3q24.3(158,048-146,295,771)x3	None
30	Stemline: 48,XY,del(1)(p32p36.1),+8,+14[2/20] Sideline 1: 47,sl,r(5)(q11.2p15.3),-7[8/20] Sideline 2: 47,sdl1,del(12)(p11.2p13)[2/20]	<ul style="list-style-type: none"> - 1p36.22p35.1(9,368,485-32,450,276)x1-2 - 2q33.3q34(208,743,984-211,927,188) hmz - 3q22.2q23(135,607,906-138,854,718) hmz - 5q22.3q35.3(114,380,344-180,719,789)x1-2 - 7p22.3q36.3(43,360-159,119,707)x1-2 	LOH on 2q including <i>MAP2</i> and <i>IDH1</i> . LOH on 3q included <i>FOXL1</i> and <i>FAIM</i> .
31	43-46,XX,-5,-7,add(7)(q11),-17,add(17)(p11)[7/20]	Normal study	None
32	45,XY,-7[17/20]	<ul style="list-style-type: none"> - 7p22.3q36.3(43,360-159,119,707)x1-2 - 11q12.3q25(63,180,135-134,942,626) mos hmz 	Mosaic CN-LOH on most of 11q including <i>CBL</i> .
33	Stemline: 45,XX,-18 [3/20] Sideline: 44,idem,der(2)t(2;6)(q21;q11),add(4)(q25),6,der(8)t(2;8)(q21;q24.?) [17/20]	<ul style="list-style-type: none"> - 3p26.2p26.1(3,899,790-4,183,674)x1 - 4q24q35.2(102,892,996-190,957,473)x1-2 - 6p25.3p22.3(156,974-24,957,511)x1-2 - 18p11.32q23(136,226-78,014,123)x1-2 	Large loss on 6p. Likely constitutional small loss on 3p.
34	47,XX,t(1;4)(p36;p12),der(6)t(6;15)(p23;q13),add(7)(q11.2),+11,-15,+22 per outside report.	<ul style="list-style-type: none"> - 7q21.3q36.1(93,084,664-151,033,762)x1-2 - 9q21.33q22.33(90,124,740-101,371,666)x1-2 - 11p15.5q25(230,615-134,938,470)x2-3 	Large loss on 9q involving <i>SYK</i> and <i>FANCC</i> .

¹ Bold font indicates copy number variations (CNVs) detected only by CMA or those that clarified/modified the previously reported abnormalities on conventional cytogenetics or FISH.

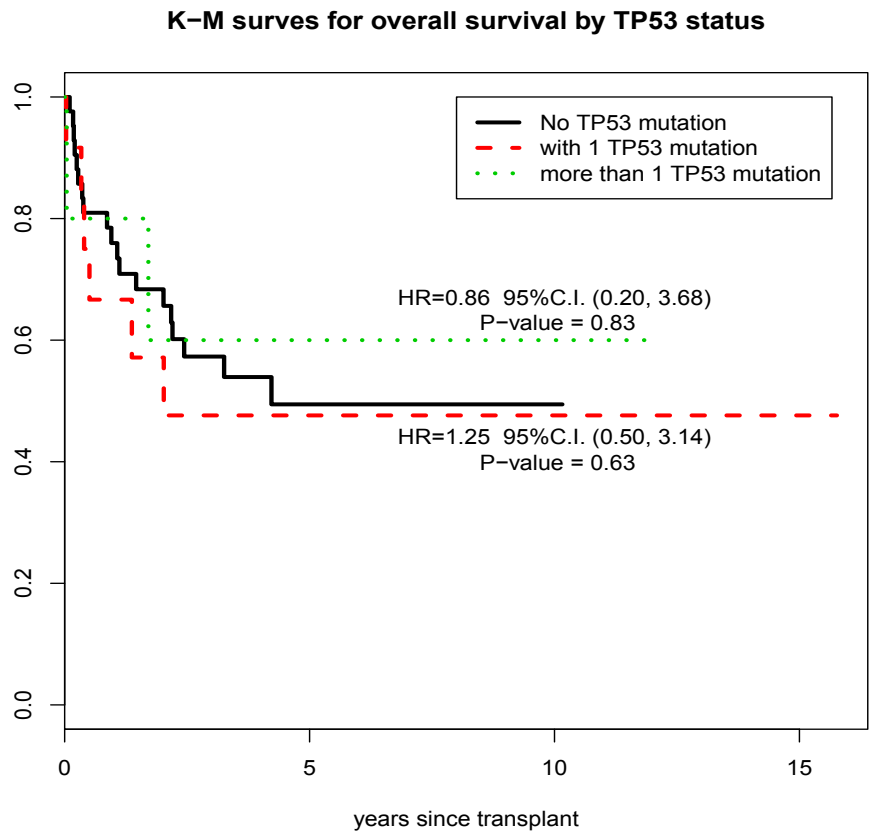
² Regular font indicates CMA detected previously reported abnormalities.

³ Hmz is referred to copy-neutral loss of heterozygosity (CN-LOH)

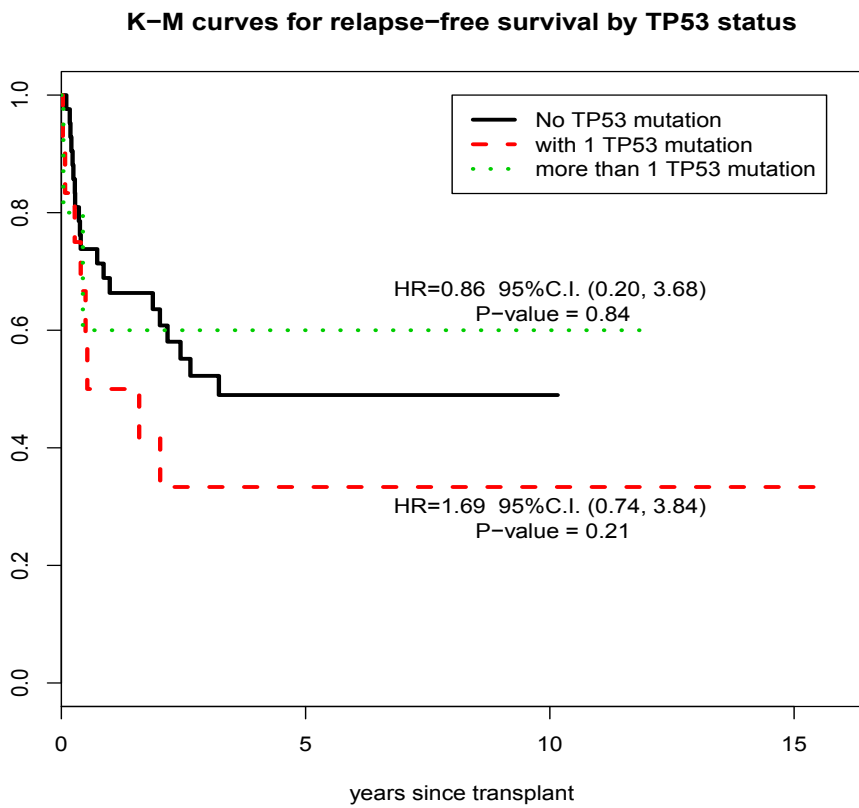
Supplement figure 1- TP53 mutation plot



Supplement figure 2a- OS by number of TP53 mutations



Supplement figure 2b- RFS by number of TP53 mutations



Supplement figure 3- t-MDS cases undergone CMA analysis (n=34)

■ CMA with added value (N=24) ■ CMA without added value (N=10)

